

600-1-200NCIP

(Sheet 1 of 26)

CAG ATG GAT CCT AAT AGA ATA TCA GAA GAT GGC ACT CAC TGC ATT TAT Gln Met Asp Pro Asn Arg Ile Ser Glu Asp Gly Thr His Cys Ile Tyr	48
1 5 10 15	
AGA ATT TTG AGA CTC CAT GAA AAT GCA GAT TTT CAA GAC ACA ACT CTG Arg Ile Leu Arg Leu His Glu Asn Ala Asp Phe Glu Asp Thr Thr Leu	96
20 25 30	
GAG AGT CAA GAT ACA AAA TTA ATA CCT GAT TCA TGT AGG AGA ATT AAA Glu Ser Gln Asp Thr Lys Leu Ile Pro Asp Ser Cys Arg Arg Ile Lys	144
35 40 45	
CAG GCC TTT CAA GGA GCT GTG CAA AAG GAA TTA CAA CAT ATC GTT GGA Gln Ala Phe Gln Gly Ala Val Gln Lys Glu Leu Gln His Ile Val Gly	192
50 55 60	
TCA CAG CAC ATC AGA GCA GAG AAA GCG ATG GTG GAT GGC TCA TGG TTA Ser Gln His Ile Arg Ala Glu Lys Ala Met Val Asp Gly Ser Trp Leu	240
65 70 75 80	
GAT CTG GCC AAG AGG AGC AAG CTT GAA GCT CAG CCT TTT GCT CAT CTC Asp Leu Ala Lys Arg Ser Lys Leu Glu Ala Gln Pro Phe Ala His Leu	288
85 90 95	
ACT ATT AAT GCC ACC GAC ATC CCA TCT GGT TCC CAT AAA GTG AGT CTG Thr Ile Asn Ala Thr Asp Ile Pro Ser Gly Ser His Lys Val Ser Leu	336
100 105 110	
TCC TCT TGG TAC CAT GAT CGG GGG TGG CGT AAG ATC TCC AAC ATG ACT Ser Ser Trp Tyr His Asp Arg Gly Trp Gly Lys Ile Ser Asn Met Thr	384
115 120 125	
TTT AGC AAT GGA AAA CTA ATA GTT AAT CAG GAT GGC TTT TAT TAC CTG Phe Ser Asn Gly Lys Leu Ile Val Asn Gln Asp Gly Phe Tyr Tyr Leu	432
130 135 140	
TAT GCC AAC ATT TGC TTT CGA CAT CAT GAA ACT TCA GGA GAC CTA GCT Tyr Ala Asn Ile Cys Phe Arg His His Glu Thr Ser Gly Asp Leu Ala	480
145 150 155 160	
ACA GAG TAT CCT CAA CTA ATG GTG TAC GTC ACT AAA ACC AGC ATC AAA Thr Glu Tyr Leu Gln Leu Met Val Tyr Val Thr Lys Thr Ser Ile Lys	528
165 170 175	
ATC CCA AGT TCT CTT ACC CTG ATG AAA GGA GGA AGC ACC AAG TAT TGG Ile Pro Ser Ser His Thr Leu Met Lys Gly Ser Thr Lys Tyr Trp	576
180 185 190	
TCA GGG AAT TCT GAA TTC CAT TTT TAT TCC ATA AAC GTT GGT GGA TTT Ser Gly Asn Ser Glu Phe His Phe Tyr Ser Ile Asn Val Gly Gly Phe	624
195 200 205	
TTT AAG TTA CGG TCT GGA GAG GAA ATC ACC ATC GAG GTC TCC AAC CCC Phe Lys Leu Arg Ser Gly Glu Glu Ile Ser Ile Glu Val Ser Asn Pro	672
210 215 220	
TCC TTA CTG GAT CCG GAT CAG GAT GCA ACA TAC TTT GGG GCT TTT AAA Ser Leu Leu Asp Pro Asp Gln Asp Ala Thr Tyr Phe Gly Ala Phe Lys	720
225 230 235 240	

Figure 1

GTT CGA GAT ATA GAT TGA GCCCCAGTTT TTGGAGTGT ATGTATTC	768
Val Arg Asp Ile Asp *	
245	
TGGATGTTTG GAAACATTTT TTAAAACAAG CCAAGAAAGA TGTATATAGG TGTGTGAGAC	828
TACTAAGAGG CATGGCCAA CGGTACACGA CTCAGTATCC ATGCTCTTGA CCTTGTAGAG	888
AACACGCGTA TTTACAGCCA GTGGGAGATG TTAGACTCAT GGTGTGTTAC ACAATGGTT	948
TTAAATTTTG TAATGAATTTC CTAGAATTAA ACCAGATTGG AGCAATTACG GGTTGACCTT	1008
ATGAGAAACT GCATGTGGGC TATGGGACGGG GTGGTCCCT GGTCTATGTGC CCCTTCGCAG	1068
CTGAAGTGGA GAGGGTGTCA TCTAGCGCAA TTGAAGGATC ATCTGAAGGG GCAAATTCTT	1128
TTGAATTGTT ACATCATGCT GGAACCTGCA AAAAATACTT TTTCTAATGA GGAGAGAAAA	1188
TATATGTATT TTTATATAAT ATCTAAAGTT ATATTTCAGA TGTATGTTT TCTTTGCAAA	1248
GTATTGTAAA TTATATTTGT GCTATAGTAT TTGATTCAAA ATATTTAAAA ATGTCTTGCT	1308
GTGACATAT TTAATGTTTT AAATGTACAG ACATATTAA CTGGTGCACT TTGTAATTC	1368
CCTGGGAAA ACTTGCAGCT AAGGAGGGGA AAAAATGTIG TTTCTTAATA TCAAATGCAG	1428
TATATTCTT CGTCTTTTT AAGTTAATAG ATTTTTCAAG ACTTGTCAAG CCTGTGCAAA	1488
AAAATTAAAA TGGATGCCTT GAATAATAAG CAGGATGTG GCCACCAGGT GCCTTCAAA	1548
TTTAGAAACT AATTGACTTT AGAAAGCTGA CATTGCCAAA AAGGATACAT AATGGGCCAC	1608
TGAAATCTGT CAAGAGTAGT TATATAATTG TTGAACAGGT GTTTTCCAC AAGTGCCGCA	1668
AATTGTACCT TTTTTGTTT TTTTCAAAAT AGAAAAGTTA TTAGTGGTTT ATCAGCAAA	1728
AAGTCCAATT TTAATTAGT AAATGTTATC TTATACTGTA CAATAAAAAC ATTGCCTT	1788
AATGTTAATT TTTGGTACA AAAGTCGACG GCCCG	1823

Figure 1 (continued)

Gln Met Asp Pro Asn Arg Ile Ser Glu Asp Gly Thr His Cys Ile Tyr  
 1 5 10 15  
 Arg Ile Leu Arg Leu His Glu Asn Ala Asp Phe Gln Asp Thr Thr Leu  
 20 25 30  
 Glu Ser Gln Asp Thr Lys Leu Ile Pro Asp Ser Cys Arg Arg Ile Lys  
 35 40 45  
 Gln Ala Phe Gln Gly Ala Val Gln Lys Glu Leu Gln His Ile Val Gly  
 50 55 60  
 Ser Gln His Ile Arg Ala Glu Lys Ala Met Val Asp Gly Ser Trp Leu  
 65 70 75 80  
 Asp Leu Ala Lys Arg Ser Lys Leu Glu Ala Gln Pro Phe Ala His Leu  
 85 90 95  
 Thr Ile Asn Ala Thr Asp Ile Pro Ser Gly Ser His Lys Val Ser Leu  
 100 105 110  
 Ser Ser Trp Tyr His Asp Arg Gly Trp Gly Lys Ile Ser Asn Met Thr  
 115 120 125  
 Phe Ser Asn Gly Lys Leu Ile Val Asn Gln Asp Gly Phe Tyr Tyr Leu  
 130 135 140  
 Tyr Ala Asn Ile Cys Phe Arg His His Glu Thr Ser Gly Asp Leu Ala  
 145 150 155 160  
 Thr Glu Tyr Leu Gln Leu Met Val Tyr Val Thr Lys Thr Ser Ile Lys  
 165 170 175  
 Ile Pro Ser Ser His Thr Leu Met Lys Gly Gly Ser Thr Lys Tyr Trp  
 180 185 190  
 Ser Gly Asn Ser Glu Phe His Phe Tyr Ser Ile Asn Val Gly Gly Phe  
 195 200 205  
 Phe Lys Leu Arg Ser Gly Glu Ile Ser Ile Glu Val Ser Asn Pro  
 210 215 220  
 Ser Leu Leu Asp Pro Asp Gln Asp Ala Thr Tyr Phe Gly Ala Phe Lys  
 225 230 235 240  
 Val Arg Asp Ile Asp \*  
 245

Figure 2

CCCACTCCCC GGGGAGCCAC TGCCAGGACC TTTGTGAACC GGTGGGGCG GGGGCCGTGG	60
CGGAGTCTGC TCGGCGGTGG GTGGCCCGAG AAGGGAGAGA ACGATCGCGG AGCAGGGCGC	120
CCGAACCTCCG GCGGCCGCGC C ATG CGC CGG GCC AGC CGA GAC TAC GGC AAG Met Arg Arg Ala Ser Arg Asp Tyr Gly Lys	171
250 255	
TAC CTG CGC AGC TCG GAA GAG ATG GGC AGC GGC CCC GGC GTC CCA CAC Tyr Leu Arg Ser Ser Glu Met Gly Ser Gly Pro Gly Val Pro His	219
260 265 270	
GAA GGT CCG CTG CAC CCC GCG CCT TCT GCA CCG GCT CCG GCG CCG CCA Glu Gly Pro Leu His Pro Ala Pro Ser Ala Pro Ala Pro Ala Pro Pro	267
275 280 285	
CCC GCC GCC TCC CGC TCC ATG TTC CTG GCC CTC CTG GGG CTG GGA CTG Pro Ala Ala Ser Arg Ser Met Phe Leu Ala Leu Leu Gly Leu Gly Leu	315
290 295 300	
GGC CAG GTG GTC TGC AGC ATC GCT CTG TTC CTG TAC TTT CGA GCG CAG Gly Gln Val Val Cys Ser Ile Ala Leu Phe Leu Tyr Phe Arg Ala Gln	363
305 310 315 320	
ATG GAT CCT AAC AGA ATA TCA GAA GAC AGC ACT CAC TGC TTT TAT AGA Met Asp Pro Asn Arg Ile Ser Glu Asp Ser Thr His Cys Phe Tyr Arg	411
325 330 335	
ATC CTG AGA CTC CAT GAA AAC GCA GGT TTG CAG GAC TCG ACT CTG GAG Ile Leu Arg Leu His Glu Asn Ala Gly Leu Gln Asp Ser Thr Leu Glu	459
340 345 350	
AGT GAA GAC ACA CTA CCT GAC TCC TGC AGG AGG ATG AAA CAA GCC TTT Ser Glu Asp Thr Leu Pro Asp Ser Cys Arg Arg Met Lys Gln Ala Phe	507
355 360 365	
CAG GGG GCC GTG CAG AAG GAA CTG CAA CAC ATT GTG GGG CCA CAG CGC Gln Gly Ala Val Gln Lys Glu Leu Gln His Ile Val Gly Pro Gln Arg	555
370 375 380	
TTC TCA GGA GCT CCA GCT ATG ATG GAA GGC TCA TGG TTG GAT GTG GCC Phe Ser Gly Ala Pro Ala Met Met Glu Gly Ser Trp Leu Asp Val Ala	603
385 390 395 400	
CAG CGA GGC AAG CCT GAG GCC CAG CCA TTT GCA CAC CTC ACC ATC AAT Gln Arg Gly Lys Pro Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn	651
405 410 415	
GCT GCC AGC ATC CCA TCG GGT TCC CAT AAA GTC ACT CTG TCC TCT TGG Ala Ala Ser Ile Pro Ser Gly Ser His Lys Val Thr Leu Ser Ser Trp	699
420 425 430	
TAC CAC GAT CGA GGC TGG GCC AAG ATC TCT AAC ATG ACG TTA AGC AAC Tyr His Asp Arg Gly Trp Ala Lys Ile Ser Asn Met Thr Leu Ser Asn	747
435 440 445	
GGA AAA CTA AGG GTT AAC CAA GAT GGC TTC TAT TAC CTG TAC GCC AAC Gly Lys Leu Arg Val Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn	795
450 455 460	
ATT TGC TTT CGG CAT CAT GAA ACA TCG GGA AGC GTA CCT ACA GAC TAT Ile Cys Phe Arg His His Glu Thr Ser Gly Ser Val Pro Thr Asp Tyr	843
465 470 475 480	

Figure 3

CTT CAG CTG ATG GTG TAT GTC GTT AAA ACC AGC ATC AAA ATC CCA AGT Leu Gln Leu Met Val Tyr Val Val Lys Thr Ser Ile Lys Ile Pro Ser 485 490 495	891
TCT CAT AAC CTG ATG AAA GGA GGG AGC ACG AAA AAC TGG TCG GGC AAT Ser His Asn Leu Met Lys Gly Gly Ser Thr Lys Asn Trp Ser Gly Asn 500 505 510	939
TCT GAA TTC CAC TTT TAT TCC ATA AAT GTT GGG GGA TTT TTC AAG CTC Ser Glu Phe His Phe Tyr Ser Ile Asn Val Gly Gly Phe Phe Lys Leu 515 520 525	987
CGA GCT GGT GAA GAA ATT AGC ATT CAG GTG TCC AAC CCT TCC CTG CTG Arg Ala Gly Glu Ile Ser Ile Gln Val Ser Asn Pro Ser Leu Leu 530 535 540	1035
GAT CCG GAT CAA GAT GCG ACG TAC TTT GGG GCT TTC AAA GTT CAG GAC Asp Pro Asp Gln Asp Ala Thr Phe Gly Ala Phe Lys Val Gln Asp 545 550 555 560	1083
ATA GAC TGA GACTCATTTC GTGGAACATT AGCATGGATG TCCTAGATGT Ile Asp *	1132
TTGGAAACTT CTTAAAAAAAT GGATGATGTC TATACATGTG TAAGACTACT AAGAGACATG GCCACGGTG TATGAAACTC ACAGCCCTCT CTCTTGAGCC CTGTACAGGT TGTGTATATG TAAAGTCCAT AGGTGATGTT AGATTACATGG TGATTACACA ACGGTTTAC AATTTTGAA TGATTTCTTA GAATTGAACC AGATTGGAG AGGTATTCCG ATGCTTATGA AAAACTTACA CGTGAGCTAT GGAAGGGGT CACAGTCTCT GGTCTAACCC CTGGACATGT GCCACTGAGA ACCTTGAAAT TAAGAGGATG CCATGTCATT GCATAGAAAT GATAGTGTGA AGGGTTAAGT TCTTTGAAAT TGTTACATTG CGCTGGGACC TGCAAATAAG TTCTTTTTT CTAATGAGGA GAAAAAATATA TGTATTTTA TATAATGTCT AAAGTTATAT TTCAAGGTGTA ATGTTTTCTG TGCAAAGTTT TGTAAATTAT ATTTGTGCTA TAGTATTGTA TTCAAAATAT TTAAAAATGT CTCACTGTTG ACATATTAA TGTTTAAAT GTACAGATGT ATTTAATGG TGCACTTTGT AATTCCCCCTG AAGGTACTCG TAGCTAAGGG GGCAGAAATAC TGTTCTGGT GACCACATGT AGTTTATTC TTTATTCTTT TTAACCTAAT AGAGTCTTCA GACTTGTCAA AACTATGCAA GCAAAATAAA TAAATAAAA TAAAATGAAT ACCTTGAATA ATAAGTAGGA TGTTGGTCAC CAGGTGCCTT TCAAATTAG AAGCTAATTG ACTTTAGGAG CTGACATAGC CAAAAAGGAA CATAATAGGC TACTGAAATC TGTCAGGAGT ATTTATGCAA TTATTGAACA GGTGTCTTTT TTTACAAGAG CTACAAMTG TAAATTTGG TTCTTTTTT TTCCCATAGA AAATGTACTA TAGTTTATCA GCCAAAAAAC AATCCACTTT TTAATTAGT GAAAGTTATT TTATTATACT GTACAATAAA AGCATTGTCT CTGAATGTAA ATTTCAGGT ACAAAAATA AATTGTACG AAAAAAAAAA AAAAAAAA AAAAA	1192 1252 1312 1372 1432 1492 1552 1612 1672 1732 1792 1852 1912 1972 2032 2092 2152 2212 2237

Figure 3 (continued)

Met Arg Arg Ala Ser Arg Asp Tyr Gly Lys Tyr Leu Arg Ser Ser Glu  
 1 5 10 15

Glu Met Gly Ser Gly Pro Gly Val Pro His Glu Gly Pro Leu His Pro  
 20 25 30

Ala Pro Ser Ala Pro Ala Pro Ala Pro Pro Pro Ala Ala Ser Arg Ser  
 35 40 45

Met Phe Leu Ala Leu Leu Gly Leu Gly Leu Gly Gln Val Val Cys Ser  
 50 55 60

Ile Ala Leu Phe Leu Tyr Phe Arg Ala Gln Met Asp Pro Asn Arg Ile  
 65 70 75 80

Ser Glu Asp Ser Thr His Cys Phe Tyr Arg Ile Leu Arg Leu His Glu  
 85 90 95

Asn Ala Gly Leu Gln Asp Ser Thr Leu Glu Ser Glu Asp Thr Leu Pro  
 100 105 110

Asp Ser Cys Arg Arg Met Lys Gln Ala Phe Gln Gly Ala Val Gln Lys  
 115 120 125

Glu Leu Gln His Ile Val Gly Pro Gln Arg Phe Ser Gly Ala Pro Ala  
 130 135 140

Met Met Glu Gly Ser Trp Leu Asp Val Ala Gln Arg Gly Lys Pro Glu  
 145 150 155 160

Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro Ser  
 165 170 175

Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly Trp  
 180 185 190

Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val Asn  
 195 200 205

Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His His  
 210 215 220

Glu Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val Tyr  
 225 230 235 240

Val Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met Lys  
 245 250 255

Gly Gly Ser Thr Lys Asn Trp Ser Gly Asn Ser Glu Phe His Phe Tyr  
 260 265 270

Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu Ile  
 275 280 285

Ser Ile Gln Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp Ala  
 290 295 300

Thr Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp \*  
 305 310 315

Figure 4

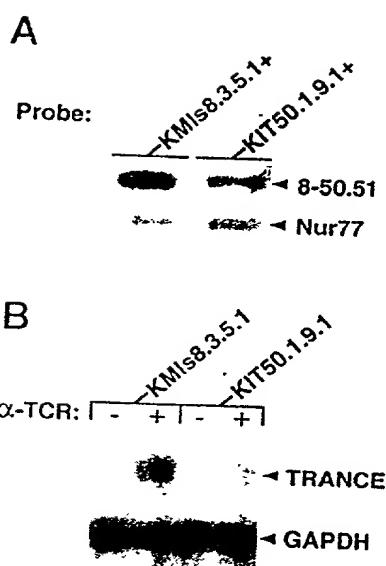


Figure 5

**A**

1 MPRASRDYGKPLKSSERGMGSGPGVPHEGPLHPAPSAAPAPPPAASRSMEIALLCLGLGQ mTRANCE  
 61 WVGSIADLFYERAQMDPNRISEDSTIICFVPIRLRUEENAGIQDSTLESEDT--LPDSCPRM mTRANCE  
 .....G....I.....DF..T....Q..KLI.....I hTRANCE  
 119 KQAFQGAVQKELQHIVGPQRFSGAPAMMEGSWLDVAQORGKPEAQPFALHTINAASIPSGS mTRANCE  
 .....S.HIRAEK..VD....L.K.S.L.....TD..... hTRANCE  
 179 HKVTLGSWYHDRGWAKISNNTLSNGKLRVNQDGFYLYANICFRHHETSGSVPTDYLLOM mTRANCE  
 ...S.....G.....F.....I.....DLA.E..... hTRANCE  
 239 VYVVKTSIKIFSSUNILMKGGTAKWWSGNSEFHFYGINVGGFFKLRACEEISIQVSNPSLL mTRANCE  
 ...T.....T.....Y.....S.....E..... hTRANCE  
 299 DPPDODATYFGAFKWWOID 716  
 .....R...

mTRANCE  
hTRANCE

**B**

120 A-GAVL-----WIVG-DORF-GAP-----MEGSWADV-----REAOPI-----I-A----- mTRANCE  
 101 Y-I-H-----F-----TOSLY-----FSEF-----I-----TSEKERS----- mfasL  
 87 Y-I-----E-----I-----I-----I-----I-----I-----I-----ITRRNSAL mTRAIL  
 93 HPQRSHASRA-----TSOCVAC-----SREFS-----WMTI-----SPFADST-----C-----COLPK-----ETDLNPE mLT-Beta  
 60 -----RDEKE-----G-----LPLI-----S-----S-----V-----P-----SSQNSS-----F-----VVAHQ----- mTNF-alpha

**B'**      **C'**      **C**      **D**

172 -----IPSGSHKVTLK-----HD-----RGWAKLISNNTLS-----K-----E-----L-----A----- mTRANCE  
 152 -----HSFSIP-----E-----DTY-----GT-----S-----V-----KYKK-----I-----E-----E----- mfasL  
 142 I-----P-----K-----K-----T-----L-----K-----E-----W-----R-----G-----H-----R----- mTRAIL  
 153 LPA-----HIL-----AWMS-----G-----I-----A-----L-----E-----R-----QFSPTH-----ALPH-----V-----L-----CH-----GY-----R mLT-Beta  
 101 -----V-----EEO-----E-----E-----C-----K-----A-----N-----I-----M-----HDLKD-----C-----P-----A-----H-----Y-----L-----K----- mTNF-alpha

**E**      **F**

223 -----PTD-----Y-----V-----V-----T-----I-----K-----G-----S-----N-----C-----STKN-----W-----SGN-----F-----F----- mTRANCE  
 199 G-----S-----N-----N-----O-----I-----N-----H-----M-----R-----N-----S-----K-----E-----I-----T-----G-----Y-----I----- mfasL  
 198 -----R-----D-----A-----R-----M-----V-----G-----S-----P-----R-----K-----L-----I-----V-----Y-----T-----G-----I----- mTRAIL  
 211 T-----I-----D-----A-----G-----A-----G-----P-----S-----P-----T-----L-----I-----A-----T-----V-----T-----W-----V-----I-----Y-----G-----I-----T mLT-Beta  
 147 G-----S-----E-----L-----T-----H-----T-----S-----F-----A-----I-----Q-----E-----K-----V-----I-----L-----S-----A-----V-----K-----A-----P-----K-----E mTNF-alpha

**G**      **H**      **I**

273 -----W-----V-----I-----K-----S-----E-----E-----E-----L-----P-----I-----D-----M-----N-----O-----D-----O-----D-----D mTRANCE  
 240 -----S-----G-----C-----E-----K-----Y-----B-----O-----L-----I-----E-----S-----K-----H-----N-----Y-----L mfasL  
 251 -----I-----C-----C-----I-----E-----K-----Y-----K-----N-----I-----F-----S-----T-----E-----M-----L-----E-----S-----M-----L-----I-----N-----L mTRAIL  
 266 -----Y-----G-----F-----E-----A-----Y-----V-----Y-----B-----D-----M-----Y-----P-----P-----K-----E-----P-----V-----M-----G mLT-Beta  
 195 P-----F-----E-----K-----D-----A-----F-----N-----L-----K-----Y-----I-----A-----E-----S-----Q-----V-----Y-----I-----V-----A-----I-----L-----A-----V-----I-----A-----L-----P-----E mTNF-alpha

Figure 6

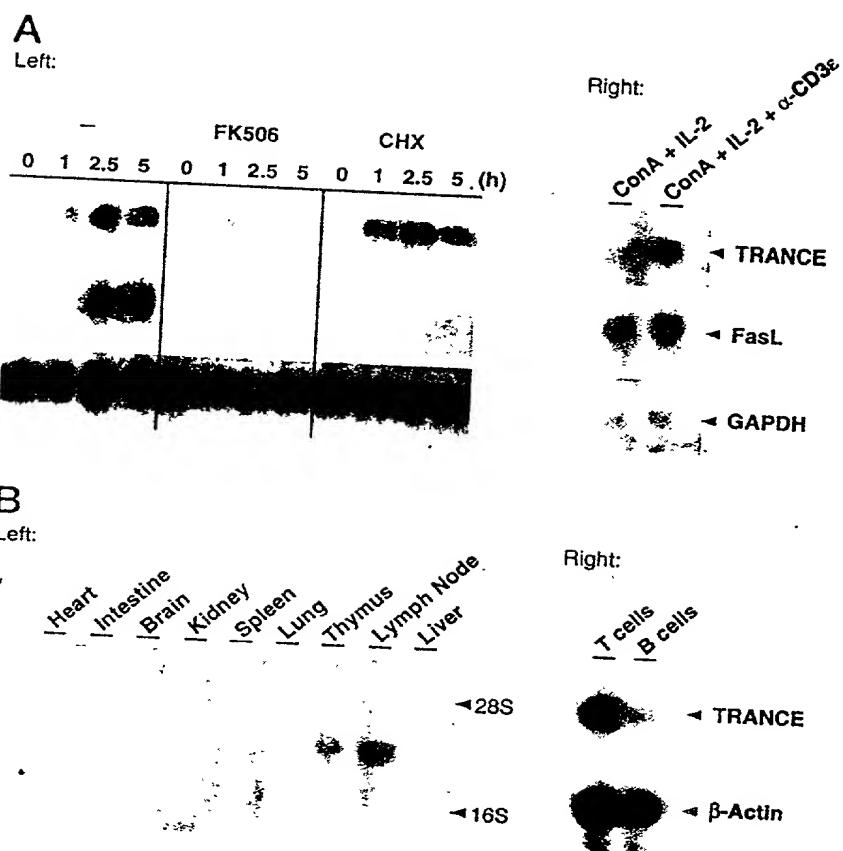
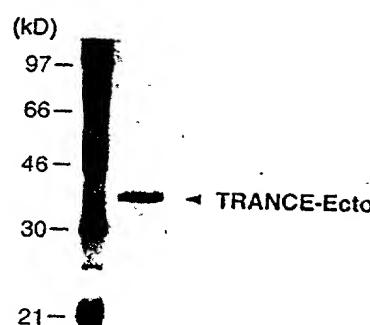
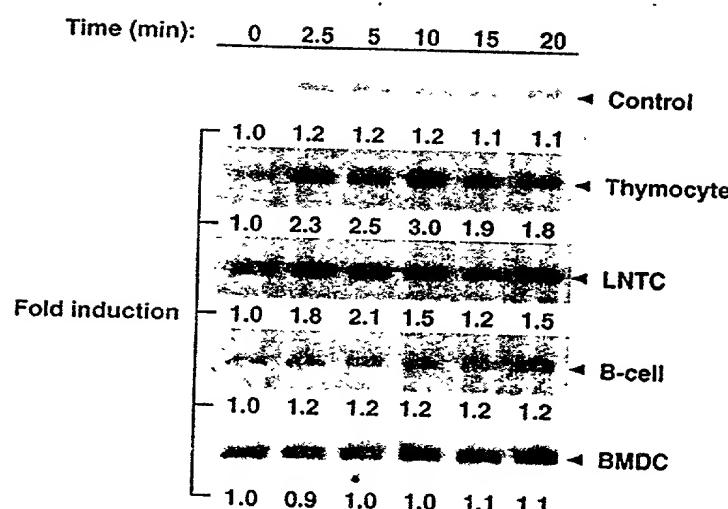


Figure 7

**A****B****Figure 8**

600-1-200W CIP

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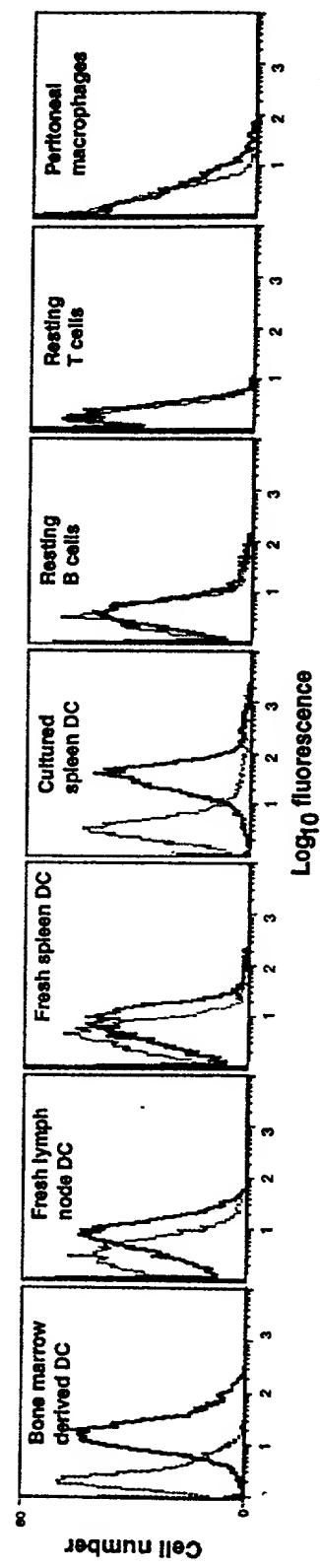


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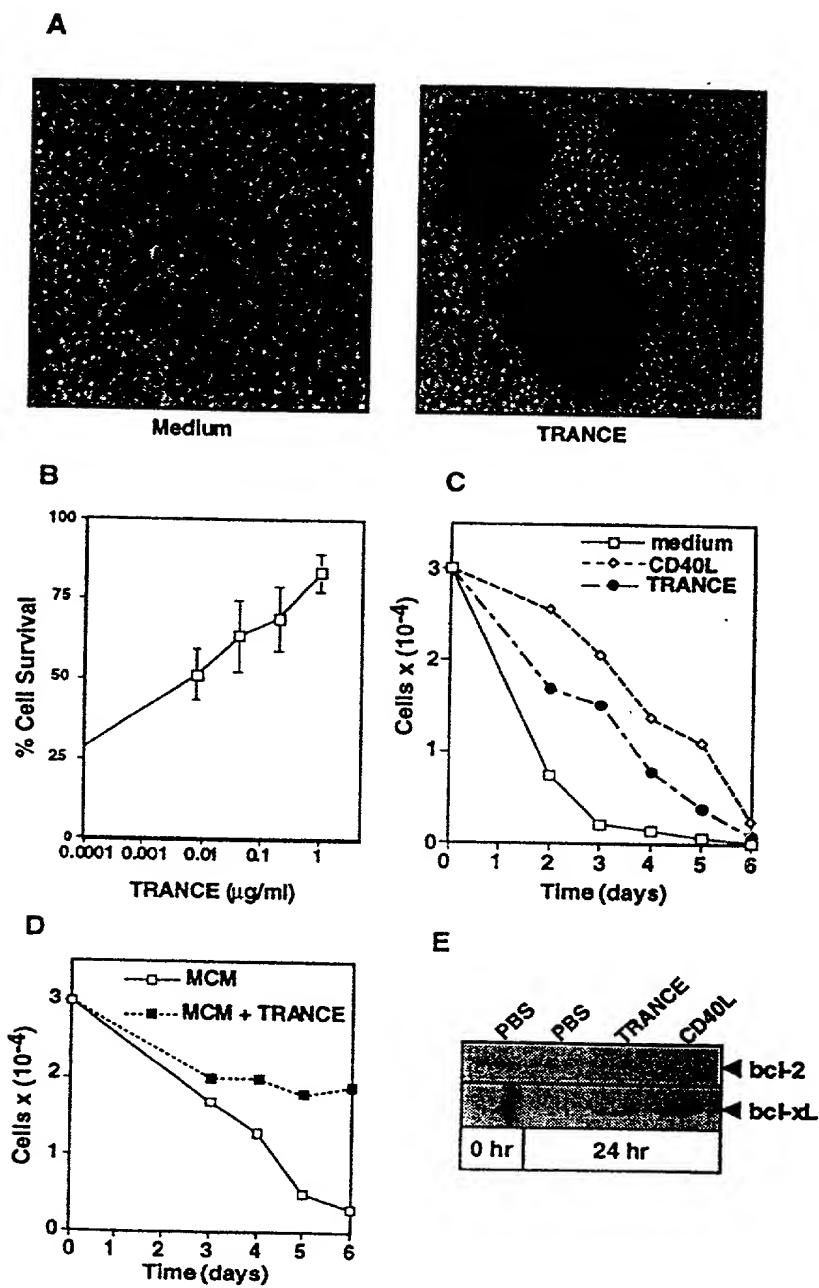


Figure 10

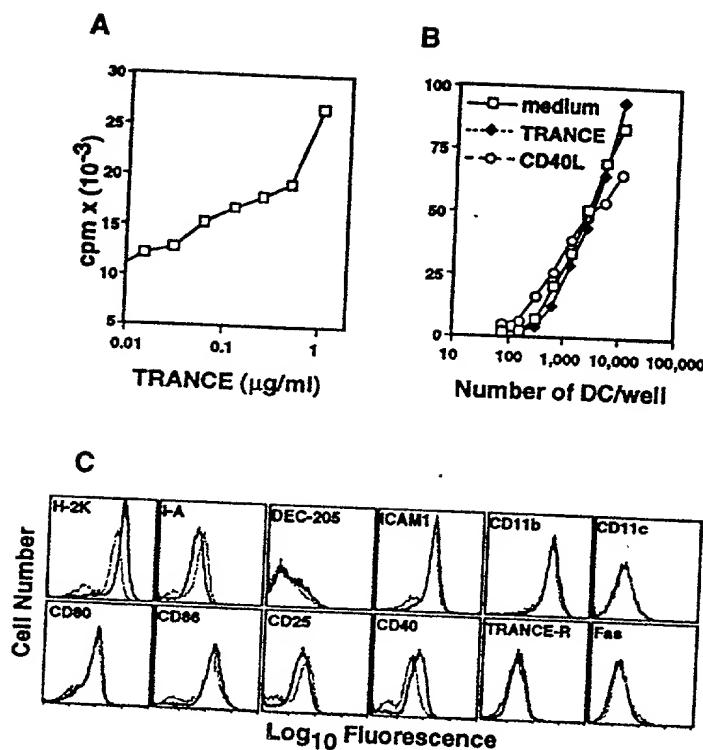


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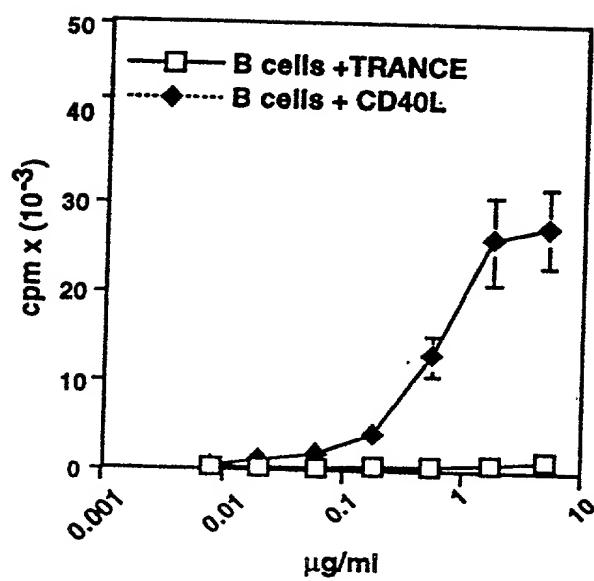


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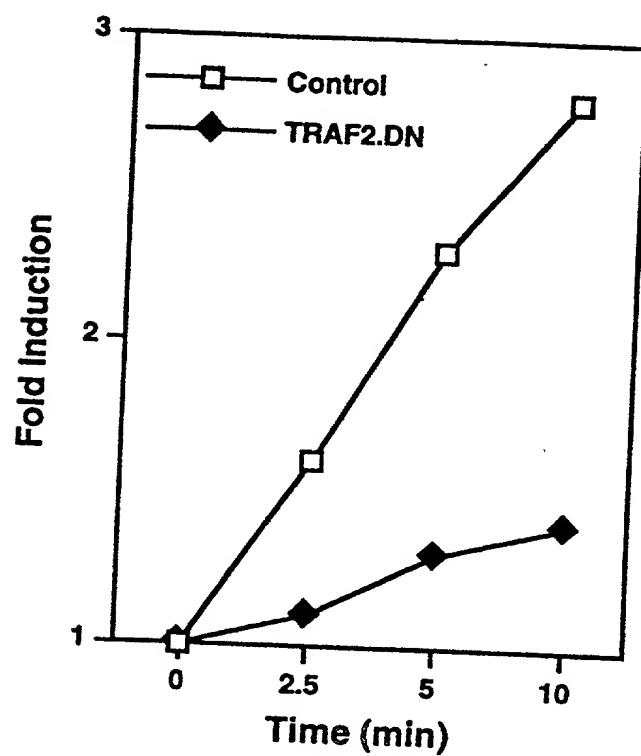


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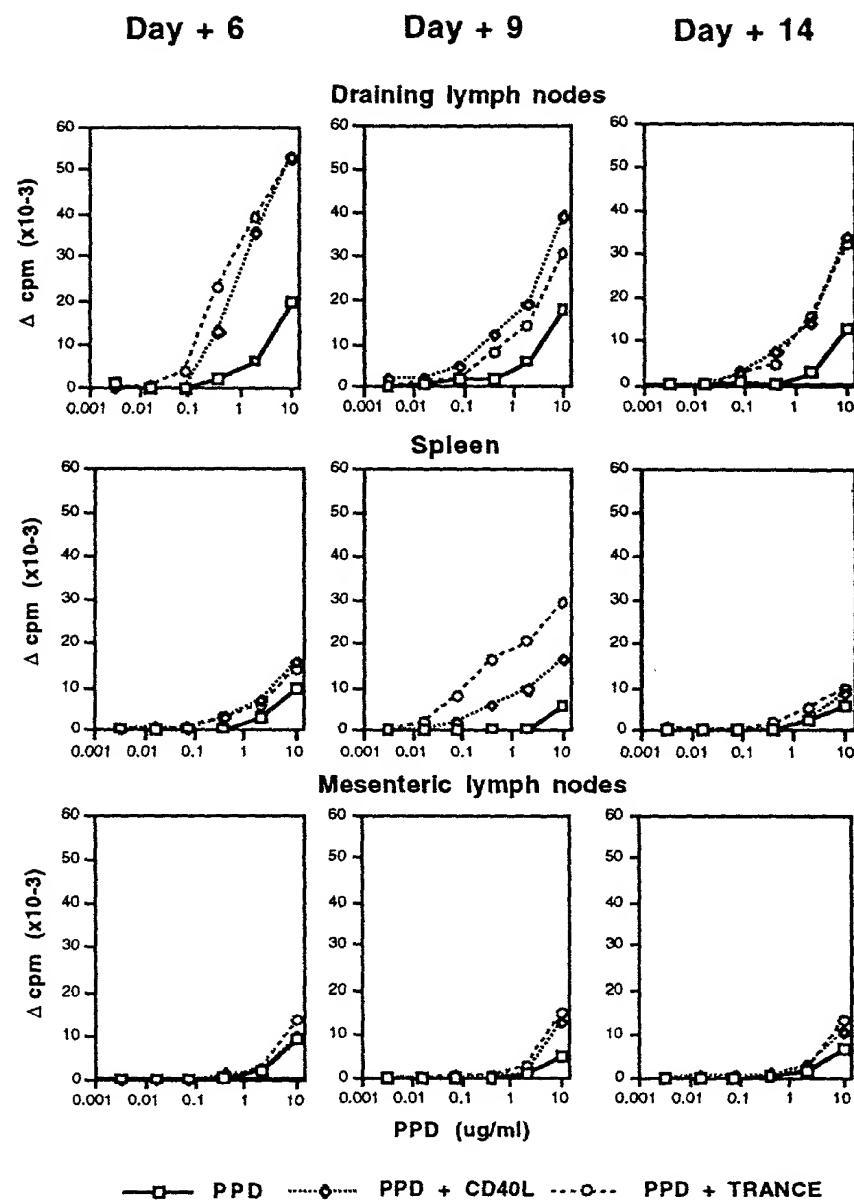


Figure 14

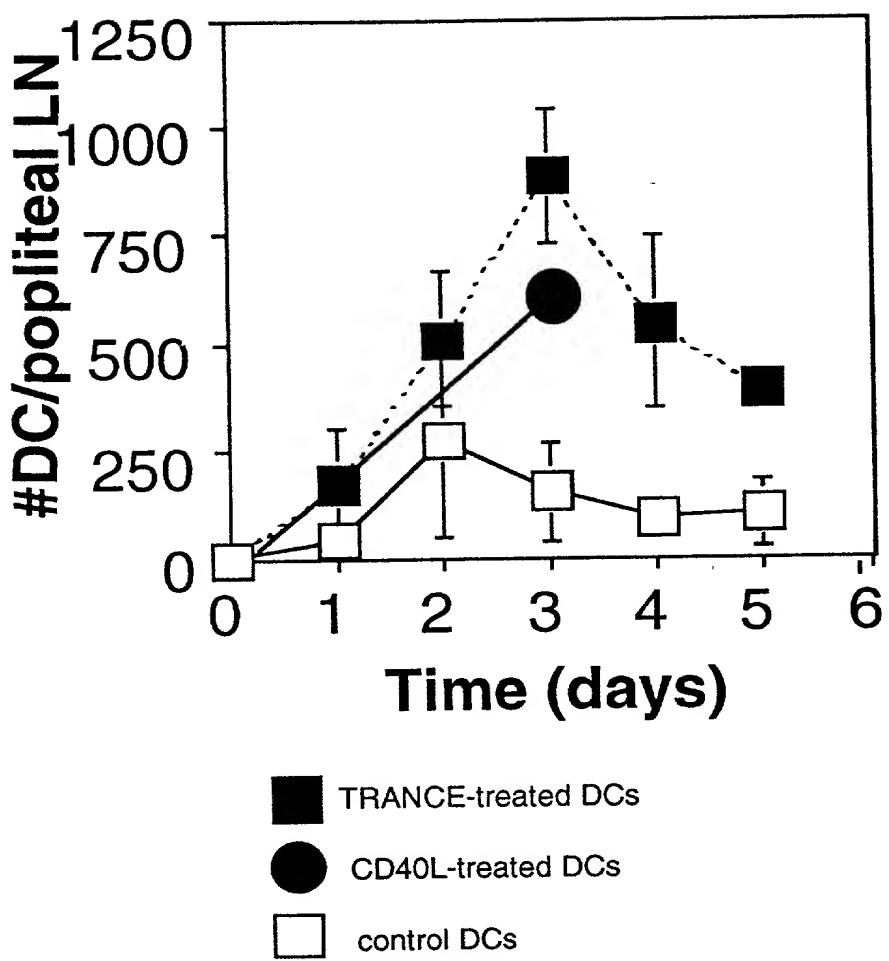


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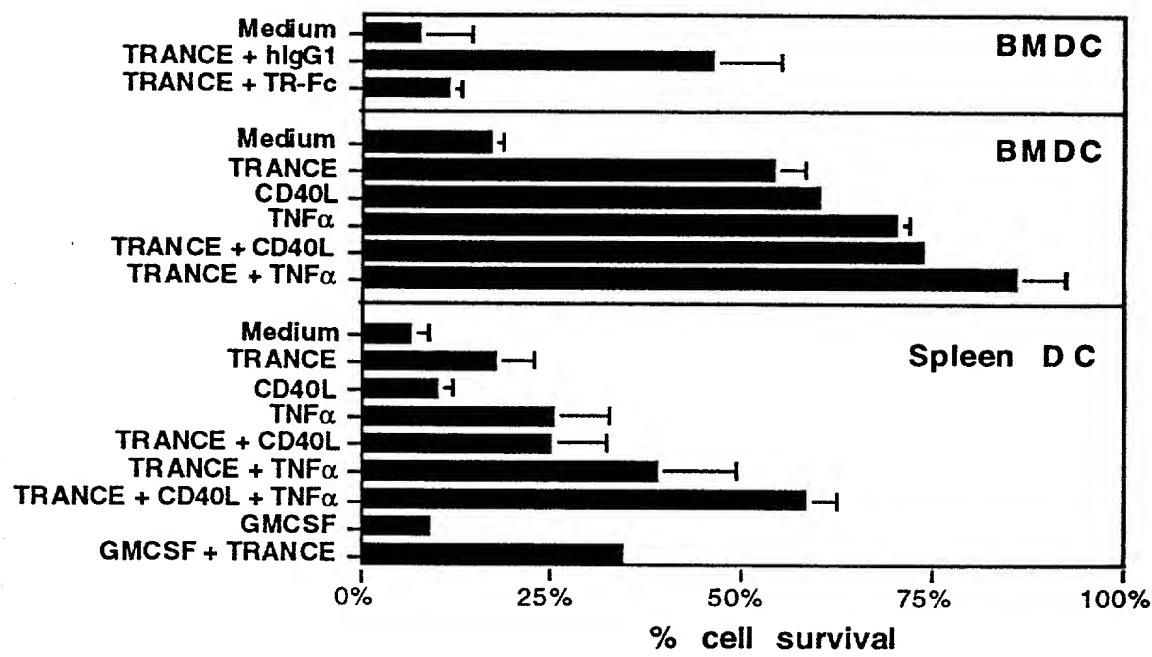


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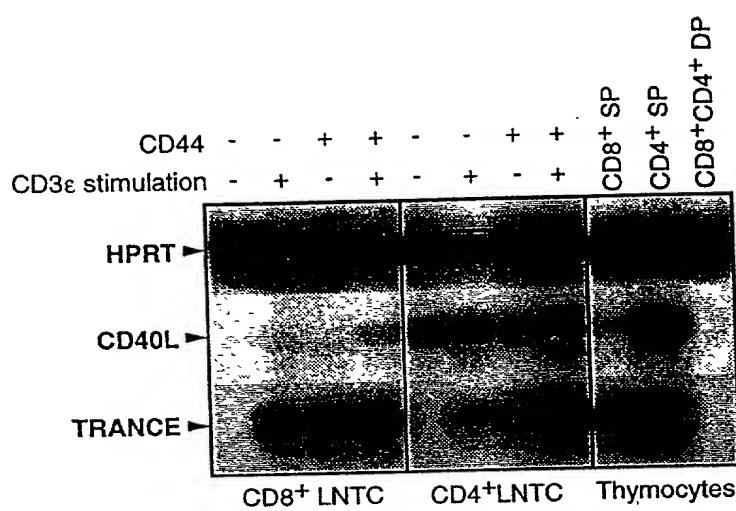


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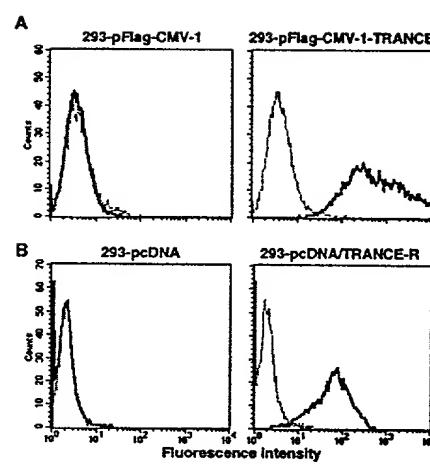


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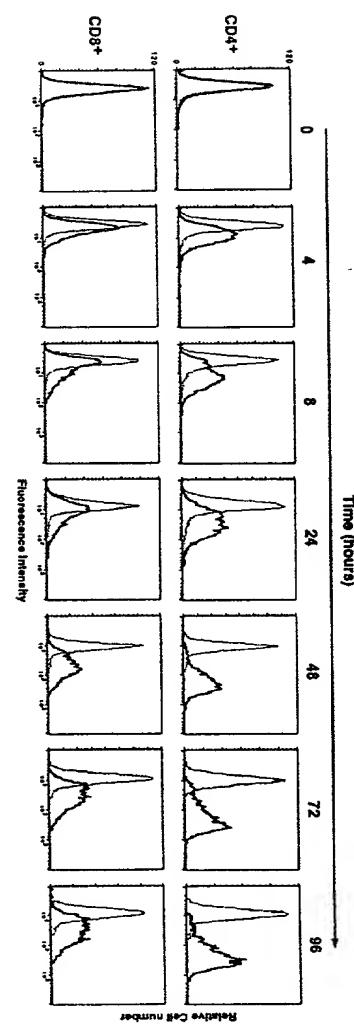


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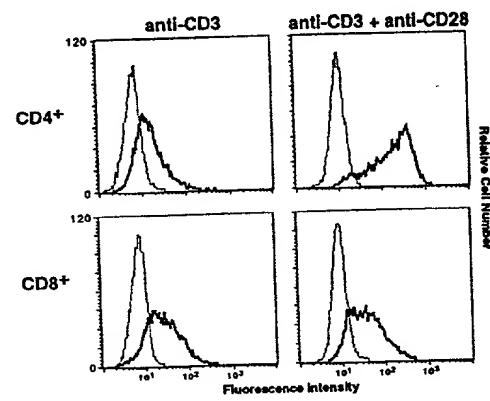


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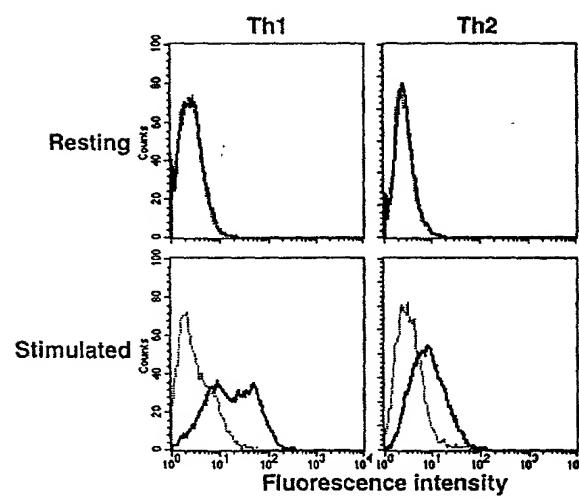


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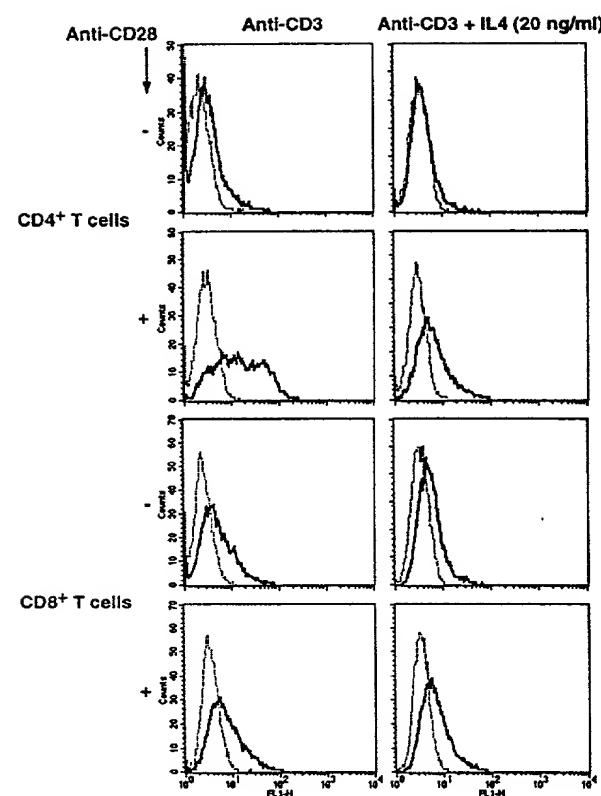


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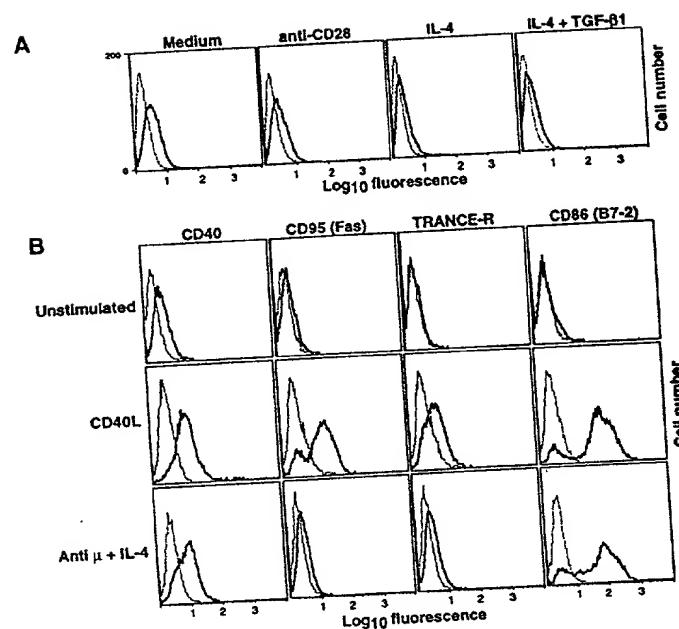


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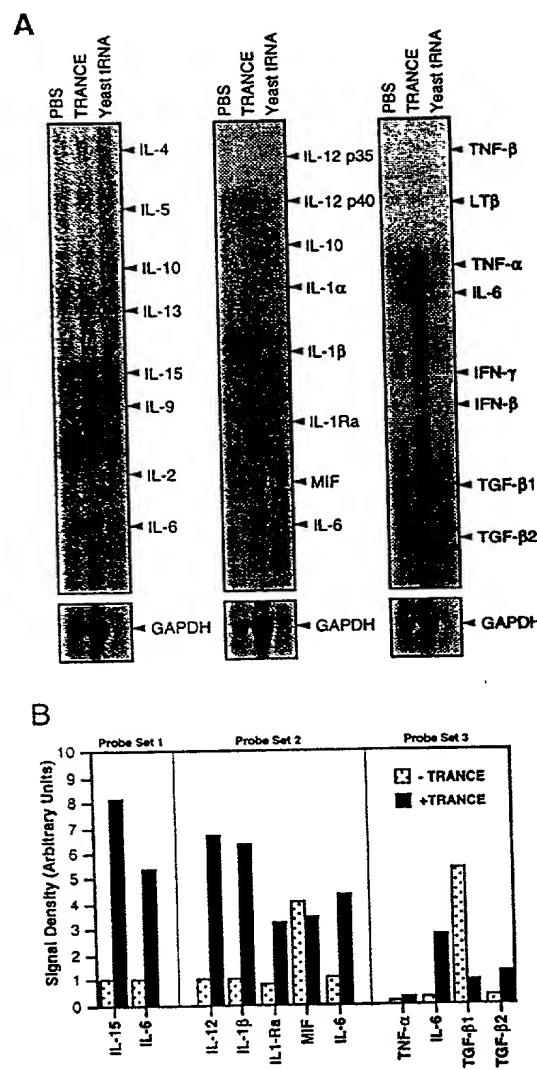


Figure 24